The *General Recommendations on Immunization* is a document that addresses issues common to more than one vaccine. It is revised by the Advisory Committee on Immunization Practice every 3-5 years as needed. The most current revision was published in February 2002 (*MMWR* 2002;51(RR-2):1-36). All providers who administer vaccine should have a copy of this document and be familiar with its contents. It can be downloaded from the *MMWR* website or ordered in print version from the National Immunization Program. This chapter discusses issues that are commonly encountered in vaccination practices.

TIMING AND SPACING OF VACCINES

The timing and spacing of vaccine doses are two of the most important issues in the appropriate use of vaccines. Specific circumstances that are commonly encountered in immunization practice are the timing of antibody-containing blood products and live vaccines (particularly measles vaccine), simultaneous and nonsimultaneous administration of different vaccines, and the intervals between subsequent doses of the same vaccine.

ANTIBODY-VACCINE INTERACTIONS

General Rule

Inactivated vaccines generally are not affected by circulating antibody to the antigen.

Live attenuated vaccines may be affected by circulating antibody to the antigen.

The presence of circulating antibody to a vaccine antigen may reduce or completely eliminate the immune response to the vaccine. The amount of interference produced by circulating antibody generally depends on the type of vaccine administered and the amount of antibody.

Inactivated antigens are not substantially affected by circulating antibody, so they can be administered before, after, or at the same time as the antibody. Simultaneous administration of antibody (in the form of immune globulin) and vaccine is recommended for postexposure prophylaxis of certain diseases, such as hepatitis B, rabies, and tetanus.

All live vaccines must replicate in order to cause an immune response. Antibody against parenteral (injected) live vaccine antigen may interfere with replication. If a live parenteral vaccine (MMR or varicella) must be given around the time that antibody is given, the two must be separated by enough time so that the antibody does not interfere with viral replication. If the live vaccine is given first, it is necessary to wait **at least 2 weeks** *(i.e.*, an incubation period) before giving the antibody. If the interval between the

Issues Regarding Spacing and Timing of Vaccines

- Interval between receipt of antibody-containing blood products and measles vaccine
- Interval between doses of different vaccines not administered simultaneously
- Interval between subsequent doses of the same vaccine

2

Antibody and Live Vaccines

Product Given First	Action
Vaccine	Wait 2 weeks before giving antibody
Antibody	Wait >3 months before giving vaccine (See Table, Appendix A)

vaccine and antibody is less than 2 weeks, the recipient should be tested for immunity or the vaccine dose should be repeated.

If the antibody is given before a dose of MMR or varicella vaccine, it is necessary to wait until the antibody has waned (degraded) before giving the vaccine to reduce the chance of interference by the antibody. The necessary interval between an antibody-containing product and MMR or varicella vaccine depends on the concentration of antibody in the product. A table listing the recommended intervals between antibody products and live vaccines (MMR and varicella) is included in Appendix A, and in the *General Recommendations on Immunization*. The interval between administration of an antibody product and MMR or varicella vaccination can be as long as 11 months.

Although passively acquired antibodies can interfere with the response to rubella vaccine, the low dose of anti-Rho(D) globulin administered to postpartum women has not been demonstrated to reduce the response to the RA27/3 strain rubella vaccine. Because of the importance of rubella immunity among childbearing age women, the postpartum vaccination of rubella-susceptible women with rubella or MMR vaccine should not be delayed because of receipt of anti-Rho(D) globulin or any other blood product during the last trimester of pregnancy or at delivery. These women should be vaccinated immediately after delivery and, if possible, tested ≥3 months later to ensure immunity to rubella and, if necessary, to measles.

Antibody for Prevention of RSV

- RSV-IG
  - –Human
  - –Contains other antibodies
- Palivizumab (Synagis)
  - –Monoclonal
  - –Contains only RSV antibody

Oral typhoid, and yellow fever vaccines are not affected by the administration of immune globulin or blood products. They may be given simultaneously with blood products, or separated by any interval. These vaccines are not affected because few North Americans are immune to yellow fever or typhoid. Consequently, donated blood products in the United States do not contain a significant amount of antibody to these organisms. The effect of circulating antibody on live attenuated influenza vaccine is not known.

Palivizumab (Synagis) contains only monoclonal antibody to respiratory synctial virus (RSV). It does not interfere with the response to live virus vaccines.

SIMULTANEOUS AND NON-SIMULTANEOUS ADMINISTRATION

General Rule

There is no contraindication to the simultaneous administration of any vaccines.

The simultaneous administration of the most widely used live and inactivated vaccines does not result in decreased antibody responses or increased rates of adverse reaction.

Simultaneous administration of all vaccines for which a child is eligible can be very important in childhood vaccination programs because it increases the probability that a child will be fully immunized at the appropriate age. A study during a recent measles outbreak showed that about one-third of measles cases in unvaccinated but vaccine-eligible preschool children could have been prevented if MMR had been administered at the same visit when another vaccine was given.

Individual vaccines should not be mixed in the same syringe unless they are licensed for mixing by the FDA. Only the Aventis-Pasteur Hib/DTaP (TriHIBit™) vaccine is licensed for mixing in the same syringe.

NONSIMULTANEOUS ADMINISTRATION OF DIFFERENT VACCINES

In some situations, vaccines that could be given simultaneously are not (*e.g.*, if the child is receiving vaccines from two different providers).

Live parenteral (injected) vaccines (MMR, varicella, and yellow fever) that are not administered simultaneously should be separated by at least 4 weeks. This precaution is intended to reduce or eliminate interference from the vaccine given first on the vaccine given later. If two live injected vaccines are not administered simultaneously but are separated by less than 4 weeks, the vaccine given second should be repeated in ≥ 4 weeks or confirmed to be effective by serologic testing of the recipient. An exception to this recommendation is yellow fever vaccine administered <4 weeks after single antigen measles vaccine. A 1999 study demonstrated that yellow fever vaccine is not affected by measles vaccine given 1-27 days earlier. The effect of nonsimultaneously administered rubella, mumps, varicella, and yellow fever vaccines is not known.

Spacing of vaccine combinations not given simultaneously

Combination	Minimum Interval
Two live parenteral	4 weeks
All other	None

Live vaccines administered by a nonparenteral route (OPV, oral typhoid, live attenuated influenza) are not believed to interfere with each other if not given simultaneously. These vaccines may be given at any time before or after each other. Oral typhoid is not licensed for children less than 6 years of age, and OPV is no longer available in the United States, so these vaccines are not likely to be given to the same child.

Spacing of live vaccines not given simultaneously

- If two live parenteral vaccines are given <4 weeks days apart the vaccine given second should be repeated.
- Exception is yellow fever vaccine given <4 weeks after measles vaccine.

Parenteral live vaccines (MMR, varicella, and yellow fever) are not believed to have an effect on live vaccines given by a nonparenteral route (OPV, oral typhoid, live attenuated influenza). Live nonparenteral vaccines may be given at any time before or after live parenteral vaccines.

All other combinations of two inactivated vaccines, or live and

inactivated vaccines may be given at any time before or after each other.

INTERVAL BETWEEN DOSES OF THE SAME VACCINE

General Rule

Increasing the interval between doses of a multidose vaccine does not diminish the effectiveness of the vaccine.

Decreasing the interval between doses of a multidose vaccine may interfere with antibody response and protection.

Minimum Intervals and Ages

Vaccine doses should not be given at intervals less than the minimum intervals or earlier than the minimum age

Immunizations are recommended for members of the youngest age group at risk for a disease for whom efficacy, immunogenicity and safety of a vaccine have been demonstrated. Most vaccines in the childhood immunization schedule require two or more doses for stimulation of an adequate and persisting antibody response. Studies have demonstrated that recommended ages and intervals between doses of the same antigen(s) provide optimal protection or have the best evidence of efficacy. Table 1 of the *General Recommendations on Immunization* (included in Appendix A, shows the recommended minimal ages and minimal intervals between immunizations for vaccines in the recommended childhood immunization schedule.

Administering doses of a multidose vaccine at shorter than the recommended intervals might be necessary in circumstances where an infant or child is behind schedule and needs to be brought up-to-date quickly or when international travel is pending. In these cases an accelerated schedule using the minimum age or minimum interval criteria can be used. Accelerated schedules should not be used routinely.

Vaccine doses should not be administered at intervals less than the recommended minimal intervals or earlier than the minimal ages. Two exceptions to this may occur. The first is for measles vaccine during a measles outbreak, when the vaccine may be administered at an age less than 12 months (this dose would not be counted, and would be repeated at >12 months of age). The second consideration involves administering a dose a few days earlier than the minimum interval or age, which is unlikely to have a substantially negative effect on the immune response to that dose. Although **vaccinations should not be scheduled at an interval or age less than the recommended minimums,** a child may have erroneously been brought to the office early, or may have come for an appointment not specifically for vaccination (for example, for an ear recheck). In this situation, the clinician can consider administering the vaccine earlier than the minimum interval or age. If the parent/child is known to the clinician and is reliable, it is preferable to reschedule the child for vaccination closer to the recommended interval. If the parent/child is not known to the clinician or is not reliable (*e.g.*, habitually misses appoint-

ments), it is preferable to administer the vaccine at that visit than to reschedule the child for a later visit which may not be kept.

Vaccine doses administered up to four days before the minimum interval or age can be counted as valid. This four day recommendation does not apply to rabies vaccine because of the unique schedule for this vaccine. Doses administered five days or earlier than the minimum interval or age should not be counted as valid doses and should be repeated as age appropriate. The repeat dose should be spaced after the invalid dose by a time greater than the recommended minimum interval shown in Table 1 of the General Recommendations. In certain situations, local or state requirements might mandate that doses of selected vaccines be administered on or after specific ages, precluding these four-day recommendations.

In some cases, a scheduled dose of vaccine may not be given on time. If this occurs, the dose should be given at the next visit. Not all permutations of all schedules for all vaccines have been studied. However, available data indicate that intervals between doses longer than those routinely recommended do not affect seroconversion rate or titer when the schedule was completed. Consequently, **it is not necessary to restart the series or add doses of any vaccine due to an extended interval between doses.** The only exception to this rule is oral typhoid vaccine in some circumstances. In the case of oral typhoid, some experts recommend repeating the series if the 4 dose series is extended to more than 3 weeks.

Violation of Minimum Intervals or Minimum Age

- ACIP recommends that vaccine doses given up to four days before the minimum interval or age be counted as valid
- Immunization programs and/or school entry requirements may not accept all doses given earlier than the minimum age or interval

Extended Interval Between Doses

- Not all permutations of all schedules for all vaccines have been studied
- Available studies of extended intervals have shown no significant difference in final titer
- It is not necessary to restart the series or add doses because of an extended interval between doses

NUMBER OF DOSES

General Rule

Live attenuated vaccines generally produce long-lasting immunity with a single dose.

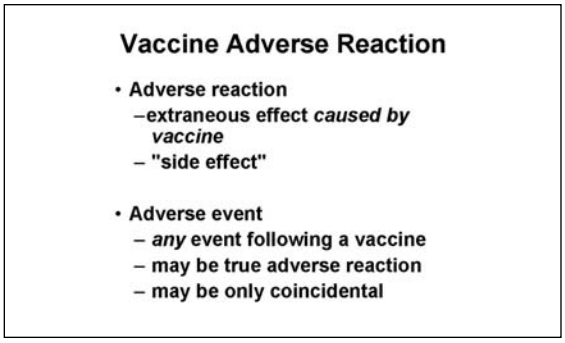
Inactivated vaccines require multiple doses and may require periodic boosting to maintain immunity.

For live injected vaccines, the first dose usually provides protection. An additional dose is given to ensure seroconversion. For instance, 95% to 98% of recipients will respond to a single dose of measles vaccine. The second dose is given to assure that nearly 100% of persons are immune (*i.e.*, the second dose is "insurance"). Immunity following live vaccines is long-lasting, and booster doses are not necessary.

For inactivated vaccines, the first dose usually does not provide protection. A protective immune response may not develop until the second or third dose. For inactivated vaccines, antibody titers may decrease ("wane") below protective levels after a few years. This phenomenon is most notable for tetanus and diphtheria. For these vaccines, periodic "boosting" is required. An additional dose is given to raise antibody back to protective levels.

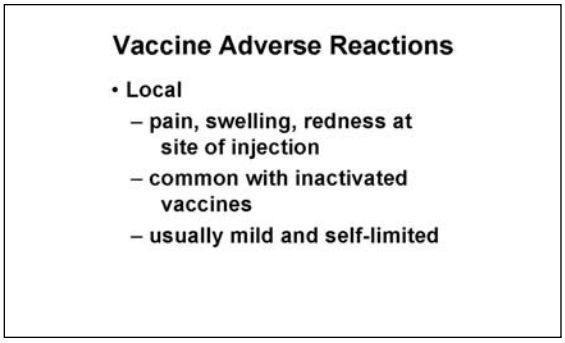
Not all inactivated vaccines require boosting throughout life. For example, Hib vaccine does not require boosting because Hib disease is very rare in children older than 5 years of age. Hepatitis B vaccine does not require boosting because of immunologic memory to the vaccine and the long incubation period of hepatitis B (which can produce an "autoboost").

ADVERSE REACTIONS FOLLOWING VACCINATION

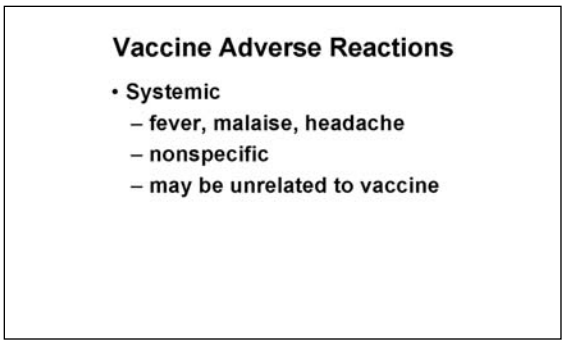


Vaccines are intended to produce active immunity to specific antigens. An **adverse reaction** is an untoward effect caused by a vaccine that is extraneous to the vaccine's primary purpose of production of immunity. Adverse reactions are also called vaccine side effects. A vaccine **adverse event** refers to *any* adverse event that occurs following vaccination. An adverse event could be a true vaccine reaction, or just a coincidental event, with further reseach needed to distinguish between them.

Vaccine adverse reactions fall into three general categories - local, systemic, and allergic. Local reactions are generally the least severe and most frequent. Allergic reactions are the most severe and least frequent.



The most common type of adverse reactions are **local reactions**, such as pain, swelling, and redness at the site of injection. Local reactions may occur in up to 50 percent of vaccine doses, depending on the type of vaccine. Local reactions are most common with inactivated vaccines, particularly those, such as DTaP, that contain adjuvants. Local adverse reactions generally occur within a few hours of the injection and are usually mild and self-limited. On rare occasions, local reactions may be very exagerated or severe. These are often referred to as hypersensitivity reactions, although they are not allergic, as the term implies. These reactions are also known as Arthus reactions, and are most commonly seen with tetanus and diphtheria toxoids. Arthus reactions are believed to be due to very high titers of antibody, usually because of too many doses of toxoid.



Systemic adverse reactions are more generalized events, and include fever, malaise, myalgias (muscle pain), headache, loss of appetite, and others. These symptoms are common and nonspecific, and may occur in a vaccinated persons because of the vaccine, or may be caused by something unrelated to the vaccine, like a concomitant viral infection.

Systemic adverse reactions were relatively frequent with whole cell DTP vaccine. However, comparison of the frequency of systemic adverse events among vaccine and placebo recipients show they are uncommon with inactivated vaccines currently in use, including acellular pertussis vaccine.

Systemic adverse reactions may occur following live attenuated vaccines. Live attenuated vaccines must replicate in order to produce immunity. The adverse reactions that follow live attenuated vaccines,

such as fever or rash represent symptoms produced from that replication, and are similar to a mild form of the natural disease. Systemic adverse reactions following live vaccines are usually mild, and occur a week or two after the vaccine was given (*i.e.*, after an incubation period of the vaccine virus). Live attenuated influenza virus replicates in the mucous membranes of the nose and throat, not in the lung. As a result, LAIV may cause upper respiratory symptoms (like a cold) but not influenza-like symptoms.

A third type of vaccine adverse reaction is a severe (anaphylactic) **allergic reaction**. The allergic reaction may be caused by the vaccine antigen itself, or some other component of the vaccine, such as cell culture material, stabilizer, preservatives, or antibiotic used to inhibit bacterial growth. Severe allergic reactions to vaccines may be life-threatening. Fortunately, they are very rare, occurring at a rate of less than one in half a million doses. The risk of an allergic reaction may be minimized by good screening prior to vaccination. All providers who administer vaccines must have an emergency protocol and supplies to treat anaphylaxis.

REPORTING VACCINE ADVERSE EVENTS

From 1978 to 1990, the CDC conducted the Monitoring System for Adverse Events Following Immunization (MSAEFI) in the public sector. In 1990, MSAEFI was replaced by the Vaccine Adverse Events Reporting System (VAERS), which includes reporting from both public and private sectors. Providers should report any clinically significant adverse event that occurs after the administration of any vaccine licensed in the United States. Providers should report any clinically significant adverse event that occurs after the administration of any vaccine licensed in the United States. Providers should report a clinically significant adverse event even if unsure whether a vaccine caused the event. The telephone number to call for answers to questions and to obtain VAERS forms is (800) 822-7967, or visit the VAERS website at http://www.vaers.org. VAERS now accepts reports of adverse reactions through their online system.

CONTRAINDICATIONS AND PRECAUTIONS TO VACCINATION

Contraindications and precautions to vaccination generally dictate circumstances when vaccines will not be given. Most contraindications and precautions are temporary and the vaccine can be given at a later time.

A **contraindication** is a condition *in a recipient* that *greatly increases* the chance of a serious adverse reaction. It is a condition in the recipient of the vaccine, not with the vaccine *per se*. If the vaccine were given in the presence of that condition, the resulting adverse reaction could seriously harm the recipient. For instance, administering influenza vaccine to a person with a true anaphylactic allergy to egg could cause serious illnes or death in the recipient. In gen-

Live Attenuated Vaccines

- Must replicate to produce immunity
- Symptoms usually mild
- Occur after an incubation period (usually 7-21 days)

Vaccine Adverse Reactions

- Allergic
  - due to vaccine or vaccine component
  - rare
  - risk minimized by screening

Contraindication

- A condition in a recipient which greatly increases the chance of a serious adverse reaction.

2

Precaution

- A condition in a recipient which may increase the chance or severity of an adverse reaction, or
- May compromise the ability of the vaccine to produce immunity.

Contraindications and Precautions

Permanent contraindications to vaccination:

- severe allergic reaction to a vaccine component or following a prior dose
- encephalopathy within 7 days of pertussis vaccination

Contraindications and Precautions

Condition	Live	Inactivated
Allergy to Component	C	C
Encephalopathy	---	C
Pregnancy	C	V
Immunosuppression	C	V
Severe illness	P	P
Recent blood product	P	V

C=contraindication P=precaution V=vaccinate if indicated

eral, vaccines should not be administered when a contraindication condition is present.

A **precaution** is similar to a contraindication. A precaution is a condition in a recipient which *may increase* the chance or severity of a serious adverse reaction, or that may compromise the ability of the vaccine to produce immunity (such as administering measles vaccine to a person with passive immunity to measles from a blood transfusion). Injury could result, but the chance of this happening is less than with a contraindication. In general, vaccines are deferred when a precaution condition is present. However, situations may arise when the benefit of protection from the vaccine outweighs the risk of an adverse reaction, and a provider may decide to give the vaccine. For example, prolonged crying or a high fever after a dose of whole cell or acellular pertussis vaccine is considered a precaution to subsequent doses of pertussis vaccine. But if the child were at high risk of pertussis exposure (*e.g.*, a pertussis outbreak in the community), a provider may choose to vaccinate the child and treat the adverse reaction if it occurs. In this example, the benefit of protection from the vaccine outweighs the harm potentially caused by the vaccine.

There are very few true contraindication and precaution conditions. Only two of these conditions are generally considered to be permanent: **severe (anaphylactic) allergy to a vaccine component or following a prior dose of a vaccine**, and **encephalopathy within 7 days of pertussis vaccination**.

Four conditions are considered permanent precautions to further doses of pertussis-containing vaccine: temperature >105^{O}F, collapse or shock-like state (hypotonic hyporesponsive episode), and persistent inconsolable crying lasting 3 or more hours occurring within 48 hours of a dose, or a seizure, with or without fever, occurring within 3 days of a dose.

Two conditions are temporary contraindications to vaccination with live vaccines: **pregnancy** and **immunosuppression**. Two conditions are temporary precautions to vaccination: **moderate or severe acute illness** (all vaccines), and **recent receipt of an antibody-containing blood product** (MMR and varicella only).

ALLERGY

A severe (anaphylactic) allergic reaction following a dose of vaccine will almost always contraindicate a subsequent dose of that vaccine. Severe allergies are those which are mediated by IgE, occur within minutes or hours of the vaccine, and require medical attention. Examples of severe allergic reactions are generalized urticaria (hives), swelling of the mouth and throat, difficulty breathing, wheezing, hypotension, or shock. With appropriate screening these reactions are very rare following vaccination. A table listing vaccine contents is included in Appendix A.

Persons may be allergic to the vaccine antigen, animal protein, antibiotics, preservatives, or stabilizers. The most common animal

protein allergen is egg protein found in vaccines prepared using embryonated chicken eggs (*e.g.*, yellow fever and influenza vaccines). **Ordinarily, persons who are able to eat eggs or egg products can receive vaccines that contain egg**; persons with histories of anaphylactic or anaphylactic-like allergy to eggs or egg proteins should not. Asking persons whether they can eat eggs without adverse effects is a reasonable way to screen for those who might be at risk from receiving yellow fever, and influenza vaccines.

Several recent studies have shown that children who have a history of severe allergy to eggs rarely have reactions to MMR vaccine. This is probably because measles and mumps vaccine viruses are both grown in chick embryo fibroblasts, not actually in eggs. It appears that it may be gelatin, not egg, that causes allergic reactions to MMR. As a result, in 1998, ACIP removed severe egg allergy as a contraindication to measles and mumps vaccines. Egg allergic children may be vaccinated with MMR without prior skin testing.

Certain vaccines contain trace amounts of **neomycin**. Persons who have experienced anaphylactic reactions to neomycin should not receive these vaccines. Most often, neomycin allergy is a contact dermatitis, a manifestation of a delayed type (cell-mediated) immune response, rather than anaphylaxis. A history of delayed type reactions to neomycin is not a contraindication for administration of these vaccines.

Latex is liquid sap from the commercial rubber tree. Latex contains naturally occurring impurities (*e.g.*, plant proteins and peptides), which are believed to be responsible for allergic reactions. Latex is processed to form natural rubber latex and dry natural rubber. Dry natural rubber and natural rubber latex might contain the same plant impurities as latex but in a lesser amounts. Natural rubber latex is used to produce medical gloves, catheters, and other products. Dry natural rubber is used in syringe plungers, vial stoppers, and injection ports on intravascular tubing. Synthetic rubber and synthetic latex also are used in medical gloves, syringe plungers, and vial stoppers. Synthetic rubber and synthetic latex do not contain natural rubber or natural latex, and therefore, do not contain the impurities linked to allergic reactions.

The most common type of latex sensitivity is contact-type (type 4) allergy, usually as a result of prolonged contact with latex-containing gloves. However, injection-procedure–associated latex allergies among diabetic patients have been described. Allergic reactions (including anaphylaxis) after vaccination procedures are rare. Only one report of an allergic reaction after administration of hepatitis B vaccine in a patient with known severe allergy (anaphylaxis) to latex has been published.

If a person reports a severe (anaphylactic) allergy to latex, vaccines supplied in vials or syringes that contain natural rubber should not be administered, unless the benefit of vaccination clearly outweighs the risk of an allergic reaction to the vaccine. For latex allergies other than anaphylactic allergies (*e.g.*, a history of contact allergy to

latex gloves), vaccines supplied in vials or syringes that contain dry natural rubber or natural rubber latex can be administered.

PREGNANCY

The concern about vaccinating pregnant women is with infection of the fetus, and is theoretical. There is no evidence that any live vaccine (including rubella) causes birth defects. See the rubella chapter for more information. However, since the theoretical possibility exists, live vaccines should not be given to women known to be pregnant.

Since inactivated vaccines cannot replicate, they cannot cause fetal infection. Inactivated vaccines should be administered to pregnant women for whom they are indicated. Susceptible household contacts of pregnant women should receive MMR and varicella vaccines.

IMMUNOSUPPRESSION

Immunosuppression

Disease

- Congenital immunodeficiency
- Leukemia or lymphoma
- Generalized malignancy

Live vaccines can cause severe or fatal reactions in immunosuppressed persons due to uncontrolled replication of the vaccine virus, particularly vaccinia and oral polio vaccine virus (and rarely measles and varicella vaccine virus). Severely immunosuppressed persons should not be given live vaccines for this reason. Persons with isolated B-cell deficiency may receive varicella vaccine. Inactivated vaccines cannot replicate, so are safe to use in immunosuppressed persons. However, response to the vaccine may be decreased.

Immunosuppression

Chemotherapy

- Alkylating agents
- Antimetabolites
- Radiation

Both diseases and drugs can cause significant immunosuppression. Persons with congenital immunodeficiency, leukemia, lymphoma, or generalized malignancy should not receive live vaccines. OPV should not be given if an immunosuppressed person is in the household. However, MMR and varicella vaccines may be given when an immunosuppressed person lives in the same house.

Certain drugs may cause immunosuppression. For instance, persons receiving cancer treatment with alkylating agents or antimetabolites, or radiation therapy should not be given live vaccines. Live vaccines can be given after chemotherapy has been discontinued for at least 3 months. Persons receiving large doses of corticosteroids should not receive live vaccines. This would include persons receiving 20 milligrams or more of prednisone daily or more than 2 milligrams of prednisone per kilogram of body weight per day.

Immunosuppression

Corticosteroids

- ≥20 mg per day
- ≥2 mg/kg per day
- NOT aerosols, topical, alternate day, short courses

Aerosolized steroids, such as inhalers for asthma, alternate day, rapidly tapering, and short (<14 days) high dose schedules, topical formulations, and physiologic replacement schedules are not contraindications to vaccination.

Inactivated vaccines are not contraindicated for immunosuppressed persons. However, response to the vaccine may be poor. A relatively functional immune system is required in order to develop an

immune response to a vaccine. An immunosuppressed person may not be protected even if the vaccine has been given. Additional recommendations for vaccination of immunosuppressed persons are detailed in the *General Recommendations on Immunization* and in a specific Altered Immunocompetence ACIP statement.

HIV INFECTION

Persons infected with human immunodeficiency virus (HIV) may have no symptoms, or may be severely immunosuppressed. In general, the same vaccination recommendations apply as with other types of immunosuppression. Live virus vaccines are usually contraindicated, and inactivated vaccines are not contraindicated.

Measles and varicella can be very severe illnesses in persons with HIV infection and are often associated with complications. Therefore, measles vaccine (as combination MMR vaccine) and varicella vaccine are recommended for persons with HIV infection who are asymptomatic or mildly immunosuppressed. However, persons with severe immunosuppression due to HIV infection should not receive measles vaccine, MMR, or varicella vaccine. Susceptible household contacts of persons with HIV infection should receive MMR and varicella vaccines. Persons with HIV infection should not receive live attenuated influenza vaccine; they should receive inactivated influenza vaccine.

Recommendations for Routine Immunization of HIV-infected Children

Vaccine	Asymptomatic	Symptomatic
Varicella	Yes	No
MMR	Yes	No
All others	Yes	Yes

Yes=vaccinate No=do not vaccinate

VACCINATION OF HEMATOPOIETIC STEM CELL TRANSPLANT RECIPIENTS

Hematopoietic stem cell transplant (HSCT) is the infusion of hematopoietic stem cells from a donor into a patient who has received chemotherapy and often radiation, both of which are usually bone marrow ablative. HSCT is used to treat a variety of neoplastic diseases, hematologic disorders, immunodeficiency syndromes, congenital enzyme deficiencies, and autoimmune disorders. HSCT recipients can receive either their own cells (*i.e.*, autologous HSCT) or cells from a donor other than the transplant recipient (*i.e.*, allogeneic HSCT).

Vaccination of Hematopoietic Stem Cell Transplant Recipients

- Includes recipients of bone marrow, peripheral cell, and umbilical cord blood transplants
- Autologous or allogeneic
- HSCT recipients should be revaccinated

Antibody titers to vaccine-preventable diseases (*e.g.*, tetanus, poliovirus, measles, mumps, rubella, and encapsulated bacteria) decline during the 1–4 years after allogeneic or autologous HSCT if the recipient is not revaccinated. HSCT recipients are at increased risk for certain vaccine-preventable diseases, including those caused by encapsulated bacteria (*i.e.*, pneumococcal and Hib infections). As a result, HSCT recipients should be routinely revaccinated after HSCT, regardless of the source of the transplanted stem cells. Revaccination with inactivated vaccines should begin 12 months after HSCT. An exception to this recommendation is for influenza vaccine, which should be administered at $\geq$6 months after HSCT and annually thereafter for the life of the recipient. MMR vaccine should be be administered 24 months after transplantation if the HSCT recipient is presumed to be immunocompetent. Varicella, meningococcal, and pneumococcal conjugate vaccines are not currently recommended for HSCT recipients because of insufficient experience using these vaccines among HSCT recipients.

Vaccination of Hematopoietic Stem Cell Transplant Recipients

- Influenza vaccine at ≥6 months following transplant and annual thereafter
- Inactivated vaccines (DTaP, Td, Hib, IPV, hepatitis B, PPV) at 12 months
- MMR at 24 months if immunocompetent
- Varicella and PCV7 vaccines not recommended (insufficient data)

Household and other close contacts of HSCT recipients and healthcare workers who care for HSCT recipients, should be appropriately vaccinated, particularly against influenza, measles, and varicella. Additional details of vaccination of HSCT recipients and their contacts can be found in a specific CDC report on this topic.

MODERATE OR SEVERE ACUTE ILLNESS

There is no evidence that a concurrent acute illness reduces vaccine efficacy or increases vaccine adverse events. The concern is that an adverse event (particularly fever) following vaccination could complicate the management of a severely ill person. If a person has a moderate or severe acute illness, vaccination with both live and inactivated vaccines should be delayed until the illness has improved.

Mild, common illnesses (such as otitis media, upper respiratory infections, colds, and diarrhea) are **NOT** contraindications to vaccination.

RECENT BLOOD PRODUCTS

Blood products may interfere with the replication of live parenteral (injected) vaccine viruses. Recent receipt of blood products is a precaution to MMR and varicella vaccines. The effect of recent receipt of blood products on live attenuated influenza vaccine is not known. Oral typhoid is not affected by circulating antibody, and blood products in the United States do not contain sufficient yellow fever antibody to interfere with replication of that vaccine. Palivizumab (Synagis) is a monoclonal antibody product used to prevent RSV infection. It contains only antibody to RSV, so will not interfere with live virus vaccination.

Varicella and MMR vaccines should be given 14 days prior to the blood product, or delayed until the antibody has degraded (see table in Appendix A, page A5). If MMR is given sooner than the minimum interval shown, the recipient should be tested for immunity or the dose repeated after the appropriate interval.

Inactivated vaccines are not substantially affected by circulating antibody from blood products and are not contraindicated.

Invalid Contraindications to Vaccination

- Mild illness
- Antibiotic therapy
- Disease exposure or convalescence
- Pregnancy in the household
- Breastfeeding
- Premature birth
- Allergies to products not in vaccine
- Family history unrelated to immunosuppression
- Need for TB skin testing
- Need for multiple vaccines

INVALID CONTRAINDICATIONS TO VACCINATION

Some healthcare providers inappropriately consider certain conditions or circumstances to be true contraindications or precautions to vaccinations. Such conditions or circumstances are known as invalid contraindications, and result in missed opportunities to administer needed vaccines. Some of the most common invalid contraindications are minor illnesses, conditions related to pregnancy and breastfeeding, allergies that are not anaphylactic in nature, and certain aspects of the patient's family history.

MINOR ILLNESS

Children with mild acute illnesses, such as low grade fever, upper respiratory infection, colds, otitis media, and mild diarrhea, can and **should be vaccinated**.

Several large studies have shown that young children with URI, otitis media, diarrhea, and/or fever respond to measles vaccine as well as those without these conditions. These large studies refute the results of an earlier small study (Krober, *JAMA* 1991) which suggested that minor infections such as URIs might impair the response to measles vaccine. Further, there is no evidence that mild diarrhea reduces the success of immunization of infants in this country.

Low grade fever is not a contraindication to immunization. Temperature measurement is not necessary before immunization if the infant or child does not appear ill and the parent does not say the child is currently ill.

ANTIBIOTIC THERAPY

Antibiotics do not have an effect on the immune response to a vaccine. No commonly used antibiotic or antiviral will inactivate a live virus vaccine.

DISEASE EXPOSURE OR CONVALESCENCE

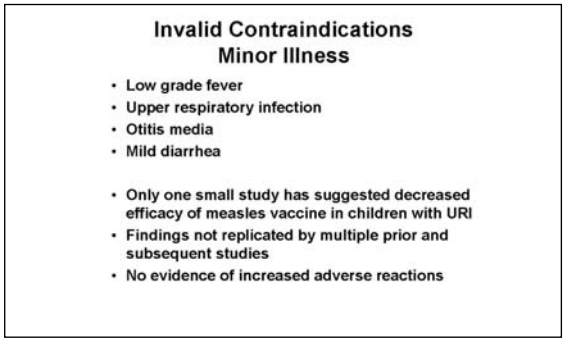
If a child is not moderately or severely ill, he or she should be vaccinated. There is no evidence that either disease exposure or convalescence will affect the response to a vaccine or increase the likelihood of an adverse event.

PREGNANCY OR IMMUNOSUPPRESSION IN THE HOUSEHOLD OR BREASTFEEDING

It is critical that healthy household contacts of pregnant women and immunosuppressed persons be vaccinated. Vaccination of healthy contacts reduces the chance of exposure of pregnant women and immunosuppressed persons.

Most vaccines, including live vaccines (MMR, varicella, and yellow fever) can be given to infants or children with pregnant or immunosuppressed household contacts, as well as to breast-feeding infants. Vaccinia (smallpox) vaccine is not recommended for persons with a pregnant or immunosuppressed household contact in non-emergency situations. Live attenuated influenza vaccine is not recommended for persons who have close contact with an immunosuppressed person, such as a healthcare worker or household contact.

Measles and mumps vaccine viruses produce a noncommunicable infection, and are not transmitted to household contacts. Rubella vaccine virus has been shown to be shed in breast milk, but transmission to an infant has rarely been documented (rubella is not trans-



mitted by mouth). Transmission of varicella vaccine virus is uncommon, and most women and older immunosuppressed persons are immune from prior chickenpox. Oral polio vaccine virus is shed and can spread, but pregnant contacts are at no greater risk than other household contacts in this situation, and OPV has not been shown to cause fetal defects. Breastfeeding does not decrease the response to routine childhood vaccines. Breastfeeding also does not extend or improve passive immunity to vaccine-preventable disease provided by maternal antibody.

PREMATURE BIRTH

Vaccines should be started on schedule based on the child's chronological age. Premature infants have been shown to respond adequately to vaccines used in infancy.

Studies demonstrate that decreased seroconversion rates might occur among certain premature infants with low birth weights (*i.e.*, <2,000 grams) after administration of hepatitis B vaccine at birth. However, by one month chronological age, all premature infants, regardless of initial birthweight or gestational age are as likely to respond as adequately as older and larger infants. All premature infants born to hepatitis B surface antigen (HBsAg) positive mothers and mothers with unknown HBsAg status must receive immunoprophylaxis with hepatitis B vaccine and hepatitis B immunoglobulin (HBIG) within 12 hours after birth. If these infants weigh less than 2000 grams at birth, the initial vaccine dose should not be counted towards completion of the hepatitis B vaccine series, and 3 additional doses of hepatitis B vaccine should be administered beginning when the infant is one month of age.

The optimal timing of the first dose of hepatitis B vaccine for premature infants of HBsAg-negative mothers with a birth weight of less than 2000 grams has not been determined. These infants can begin the first dose of the hepatitis B vaccine series at one month of chronological age. Premature infants discharged from the hospital prior to one month chronological age may also be given hepatitis B vaccine at discharge if they are medically stable and showing consistent weight gain.

NONSPECIFIC ALLERGIES, ALLERGIES TO ANTIBIOTICS NOT IN VACCINE, NONSEVERE EGG ALLERGIES, AND ALLERGIES TO DUCK ANTIGENS

Infants and children with nonspecific allergies, duck or feather allergy, allergy to penicillin, relatives with allergies, and children taking allergy shots can and should be immunized. No vaccine available in the United States contains duck antigen or penicillin.

NONANAPHYLACTIC ALLERGY TO VACCINE COMPONENT

Anaphylactic allergy to a vaccine component (such as egg or neomycin) is a true contraindication to vaccination.
Nonanaphylactic allergy to a vaccine constituent is **not** a contraindication to that vaccine.

FAMILY HISTORY OF ADVERSE REACTIONS UNRELATED TO IMMUNOSUPPRESSION, OR FAMILY HISTORY OF SEIZURES OR SIDS

The only family history that is relevant in the decision to vaccinate a child is immunosuppression, and only for oral poliovirus vaccine. OPV should not be given to a child with a personal or family history of immunosuppression, because the vaccine virus could spread to the immunosuppressed contact.

NEED OR REQUIREMENT FOR TUBERCULOSIS SKIN TEST (PPD)

Infants and children who need TB skin tests can and should be immunized. All vaccines, including MMR, can be given on the **same day** as a TB skin test, or **any time after a TB skin test is applied.** For most vaccines, there are no TB skin test timing restrictions at all.

MMR vaccine may decrease the response to a TB skin test, potentially causing a **false negative** response in someone who actually has an infection with tuberculosis. MMR can be given the same day as a TB skin test, but if MMR has been given and one or more days have elapsed, in most situations it is recommended to wait 4-6 weeks before giving a routine TB skin test. No information on the effect of varicella vaccine on a TB skin test is available. Until such information is available, it is prudent to apply rules for spacing measles vaccine and TB skin testing to varicella vaccine.

SCREENING FOR CONTRAINDICATIONS AND PRECAUTIONS TO VACCINATION

The key to preventing serious adverse reactions is screening. **Every person who administers vaccines should screen every patient for contraindications and precautions before giving the vaccine dose.** Effective screening is not difficult or complicated and can be accomplished with just a few questions.

How is your child (or how are you) today?
This question screens for concurrent moderate or acute illness. If the child has been examined, this question may not be necessary, or may have already been asked.

Does your child have any allergies to any food or medication?
A severe allergy to a vaccine component is a contraindication to vaccination, so this question must always be asked. It may be more time-efficient to inquire about allergies in a generic way (*i.e.*, any food or medication), rather than to inquire about specific vaccine components. Most parents will not be familiar with minor components of vaccine, but they should know if the child has had an allergic reaction to a food or medication severe enough to require medical attention.

Screening Questions

- Allergies to food or medication?
- How is your child today?
- Any problem after last shots?

Did the child have any problems after his or her last shots?
This open-ended question explores for allergic reactions to previous doses, and for conditions following pertussis vaccine that may be precautions to additional doses, such as high fever or a hypotonic episode.

Does the child have any problems with his or her immune system?
This question will help identify children with immunodeficiency who generally should not receive live attenuated vaccines, particularly oral polio vaccine.

Does anyone in your household have a problem with their immune system?
Oral polio vaccine and live attenuated influenza vaccine should not be given to a healthy person who has household contact with someone who is immunodeficient.

Has the child received any blood products in the last year, like a transfusion, or immune globulin?
This question helps identify precautions for live attenuated MMR and varicella vaccines, which should not be given to persons who have received passive antibody in the last few months. The question may also expose unreported illnesses that might not have been revealed in earlier questions.

Are you pregnant, or trying to become pregnant?
This question should be asked of **all adolescent and adult women.** MMR and varicella vaccines should not be given to women known to be pregnant or for 4 weeks prior to pregnancy. It is not necessary to inquire about pregnancy in household contacts because a pregnant woman in the household is not a contraindication for administration of any vaccine. ACIP does not recommend pregnancy testing prior to administration of any vaccine.

Every person should be screened for contraindications and precautions prior to vaccination. Standardized screening forms for both children and adults, developed by the Immunization Action Coalition, are included in Appendix A.

Screening Questions

- Problems with immune system?
- Anyone in household with immune problems?
- Blood products in last year?
- Pregnant?

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